IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AMARIN PHARMA, INC., AMARIN PHARMACEUTICALS IRELAND LIMITED, MOCHIDA PHARMACEUTICAL CO., LTD., Plaintiffs, v. HIKMA PHARMACEUTICALS USA INC., HIKMA PHARMACEUTICALS PLC, Defendants.	C.A. No. _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT AND DEMAND FOR JURY TRIAL

Plaintiffs Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited ("Amarin") and Mochida Pharmaceutical Co., Ltd. ("Mochida") (collectively, "Plaintiffs"), by their attorneys, hereby allege as follows:

THE NATURE OF THE ACTION

1. This is an action for infringement of U.S. Patent Nos. 9,700,537 ("the '537 patent"), 8,642,077 (the "'077 patent"), and 10,568,861 (the "'861 patent") (collectively, the Asserted Patents") under the Patent Laws of the United States, 35 U.S.C. § 100 et seq., including § 271(b). In violation of these laws, Defendants are marketing their generic version of Amarin's ground-breaking VASCEPA® product to reduce the risk of cardiovascular events such as heart attack and stroke ("cardiovascular risk reduction"). VASCEPA® is the first and only innovative omega-3 acid-based product approved for cardiovascular risk reduction by the United States Food and Drug Administration.

THE PARTIES

2. Amarin Pharma, Inc. is a company organized under the laws of Delaware with its principal place of business at 440 Route 22, Suite 330, Bridgewater, NJ 08870.

3. Amarin Pharmaceuticals Ireland Limited is a company incorporated under the laws of Ireland with registered offices at 88 Harcourt Street, Dublin 2, Dublin, Ireland.

4. Mochida Pharmaceutical Co., Ltd. is a company incorporated under the laws of Japan with its principal place of business at 1-1, Ichigayahonmuracho, Shinjuku-ku, Tokyo 162-0845, Japan.

5. On information and belief, Defendant Hikma Pharmaceuticals USA Inc. is a corporation organized and existing under the laws of Delaware with its principal place of business at 246 Industrial Way West, Eatontown, NJ 07724.

6. On information and belief, Defendant Hikma Pharmaceuticals PLC is a corporation organized and existing under the laws of the United Kingdom with its principal place of business at 1 New Burlington Place, London W1S 2HR.

7. Upon information and belief, Hikma Pharmaceuticals USA Inc. is a wholly-owned subsidiary of Hikma Pharmaceuticals PLC.

8. Upon information and belief, Hikma Pharmaceuticals USA Inc. acts at the direction, and for the benefit, of Hikma Pharmaceuticals PLC, and is controlled and/or dominated by Hikma Pharmaceuticals PLC. Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals PLC are hereinafter referred to together as "Defendants" or "Hikma."

9. Upon information and belief, Defendants collaborate with respect to the development, regulatory approval, marketing, sale, and/or distribution of pharmaceutical products. On further information and belief, Defendants are agents of each other and/or operate in concert

as integrated parts of the same business group, and enter into agreements with each other that are nearer than arm's length.

10. Upon information and belief, Hikma Pharmaceuticals USA Inc. is the current owner of ANDA No. 209457 for 1g and 0.5 g icosapent ethyl capsules purportedly bioequivalent to VASCEPA®.

11. Upon information and belief, on May 21, 2020, FDA granted final approval for Defendants' 1g icosapent ethyl capsules under ANDA No. 209457.

12. Attached hereto as Exhibit A is a press release issued by Hikma Pharmaceuticals PLC on or about May 22, 2020 announcing that "Hikma Pharmaceuticals USA Inc. has received approval from the US Food and Drug Administration (FDA) for its Icosapent Ethyl Capsules, 1 gm, the generic equivalent to Vascepa®."

13. Attached hereto as Exhibit N is a press release issued by Hikma Pharmaceuticals PLC on or about November 5, 2020 announcing the launch of Hikma's icosapent ethyl capsules. On information and belief, on November 5, 2020, Hikma launched and began offering for sale and/or selling its generic icosapent ethyl capsules in the United States, including this jurisdiction.

14. Upon information and belief, Defendants act collaboratively to commercially manufacture, market, distribute, offer for sale, and/or sell Hikma's icosapent ethyl capsules in the United States, including this jurisdiction.

JURISDICTION AND VENUE

15. This Court has subject matter jurisdiction over the action under 28 U.S.C. §§ 1331 and 1338(a).

16. This Court has personal jurisdiction over Hikma Pharmaceuticals USA Inc. because it is incorporated in Delaware and thus is present in and resides in this District, and because Hikma

Pharmaceuticals USA Inc. is doing business in this District and has thus purposefully availed itself to the privileges of conducting business in Delaware.

17. Venue is proper in this District over Hikma Pharmaceuticals USA, Inc. under 28 U.S.C. § 1400(b).

18. This Court has personal jurisdiction over Hikma Pharmaceuticals PLC because, on information and belief, it manufactures, imports, offers for sale, and sells pharmaceutical drugs that are sold in the United States, including in Delaware, and derives substantial income therefrom.

19. In the alternative, this Court may exercise personal jurisdiction over Hikma Pharmaceuticals PLC pursuant to Fed. R. Civ. P. 4(k)(2) because (a) Plaintiffs' claims arise under federal law; (b) Hikma Pharmaceuticals PLC is a foreign company not subject to personal jurisdiction in the courts in any state, and (c) Hikma Pharmaceuticals PLC has sufficient contacts with the United States as a whole, including but not limited to marketing and/or selling generic pharmaceutical products that are distributed and sold throughout the United States, such that this Court's exercise of jurisdiction over Hikma Pharmaceuticals PLC satisfies due process.

20. Venue is proper in this District with respect to Hikma Pharmaceuticals PLC pursuant to 28 U.S.C. § 1391(c)(3) because it is not resident in the United States.

FACTUAL BACKGROUND

A. VASCEPA®, REDUCE-IT, JELIS and EPA's Reduction of Cardiovascular Risk

21. The three types of omega−3 fatty acids involved in human physiology are α-linolenic acid (ALA), found in plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both commonly found in marine (fish) oils.

22. Amarin and Mochida are recognized worldwide as the leading innovation-driven companies committed to the research and development of EPA-based drug products to treat the needs of millions of patients who are at risk of cardiovascular disease

23. Mochida developed and markets a prescription pure EPA drug product, Epadel, in Japan.

24. Amarin developed and markets VASCEPA®, a prescription drug that contains pure EPA, in the United States.

25. Amarin conducted a series of clinical trials to support FDA approval of VASCEPA®.

26. In the MARINE trial that led to VASCEPA®'s first approval, VASCEPA® was found to lower triglycerides in patients with severe hypertriglyceridemia (≥500 mg/dL) without raising bad cholesterol, or LDL-C, levels. Upon FDA approval in 2012, VASCEPA® became the first (and still only) approved medication for treating severe hypertriglyceridemia that does not raise LDL-C.

27. After that approval to treat severe hypertriglyceridemia, Amarin continued its clinical work towards its primary goal, approval of VASCEPA® for use in cardiovascular risk reduction. Based on an agreed protocol with the FDA, Amarin had conducted a clinical trial known as ANCHOR, in which Amarin examined VASCEPA® as an add-on to statin therapy in patients with persistent high (≥200 mg/dL and <500 mg/dL) triglycerides. As agreed with FDA, Amarin evaluated VASCEPA®'s effect on cardiovascular risk reduction based on triglyceride level lowering as a surrogate, or substitute, for cardiovascular risk reduction while awaiting the results of Amarin's REDUCE-IT trial.

28. While ANCHOR met its clinical endpoints, including the exploratory endpoint of median placebo-adjusted percent change in high-sensitivity C reactive protein (hs-CRP), *see* Ex.

U (Ballantyne), FDA's view on the use of triglyceride levels as a surrogate for cardiovascular risk changed. Ex. BB. FDA identified several clinical trials where other therapies, including other omega-3 based therapies, lowered triglyceride levels in this patient population but did not show an actual reduction in cardiovascular risk. The trials failing to show a cardiovascular risk reduction included ACCORD-Lipid, AIM-HIGH, and HPS2-THRIVE.

29. Accordingly, Amarin proceeded to complete REDUCE-IT, a trial in which the effects of VASCEPA® on cardiovascular risk reduction were evaluated directly. The REDUCE-IT study was completed by Amarin at great cost. In REDUCE-IT, Amarin followed more than 8000 patients over a median of five years and evaluated the effectiveness of VASCEPA® as an add-on to statin therapy in reducing major cardiovascular events in patients with persistent elevated triglycerides. *See* Ex. V (Bhatt).

30. The results of REDUCE-IT, first announced in 2018, *see* Ex. H, were hailed as one of the most important developments in the prevention and treatment of cardiovascular disease since statins. Compared to statins alone on top of other contemporaneous medical therapy, VASCEPA® showed a 25% reduction in major cardiovascular events such as cardiovascular death, myocardial infarction, and stroke. Based on those results, in December 2019, FDA approved VASCEPA® for a second indication as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. Ex. I. Similar to the ANCHOR results, a reduction in hs-CRP was observed in REDUCE-IT which may in part explain the cardiovascular risk benefit. *See* Ex. V (Bhatt) at 20. This is consistent with the investigators in the ANCHOR trial, who stated that one

of the potential explanations for increased cardiovascular risk might be inflammation and VASCEPA® showed a 22% reduction of hs-CRP in the mixed dyslipidemia population studied in ANCHOR. *See* Ex. U (Ballantyne); *see also* Exhibit O at col. 18, l. 11-12.

31. In a press release about this additional approval, FDA recognized that "VASCEPA is the first FDA-approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy." Ex. J. The results of REDUCE-IT were met with widespread enthusiasm and surprise in the field and have been hailed as a "game changer" in medicine. Ex. Y; Ex. Z.

32. Amarin's work in the MARINE, ANCHOR, and REDUCE-IT clinical trials was preceded by other work done by Mochida, in Japan. In the late 1990s and early 2000s, Mochida sponsored a cardiovascular outcomes trial with Epadel in Japan, called JELIS (Japanese EPA Lipid Intervention Study). JELIS was the world's first large-scale randomized controlled cardiovascular outcomes trial of a prescription pure EPA drug product. The JELIS results reported that pure EPA suppressed coronary artery disease in Japanese hypercholesterolemic patients who routinely consume a large amount of EPA and DHA (another poly unsaturated fatty acid) from fish oil in their diet.

33. A further statistical analysis of JELIS was undertaken to assess the effect of EPA on patients with a particular profile of risk factors for coronary artery disease, and reported beneficial effects of the drug in further reducing cardiovascular events in statin-treated, hypercholesterolemic Japanese patients.

34. Those effects are published in Saito et al., titled, "Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: Sub-analysis of primary

prevention cases from the Japan EPA Lipid Intervention Study (JELIS), 200 Atherosclerosis 135-400 (2008) [hereinafter, the "Saito Article"]. The Saito Article is attached hereto as Exhibit B.

35. The Saito Article reports on a statistical analysis of patients studied in the JELIS trial who had no history of coronary artery disease (i.e., the patients had not previously had a cardiovascular event). Ex. B (Saito) at § 2.1. The primary endpoint was major coronary events (MCE): sudden cardiac death, fatal myocardial infarction, nonfatal myocardial infarction, unstable angina pectoris including hospitalization for documented ischemic episodes, and angioplasty/stenting or coronary artery bypass grafting. Ex. B (Saito) at § 2.3.

36. The Saito Article reports that the "EPA treatment lowered the risk for MCE for the [studied population] by 53% (HR: 0.47; 95% CI: 0.23-0.98; $P = 0.43$; Fig. 3)." Ex. B (Saito) at 138. By comparison, MCE risk was reduced by 18% in all primary prevention subjects treated in the JELIS clinical study. Ex. B (Saito) at 139.

B. The Asserted Patents

37. On July 11, 2017, the United States Patent and Trademark Office ("USPTO") duly and legally issued the '537 patent, titled "Composition for Preventing the Occurrence of Cardiovascular Event in Multiple Risk Patient," and naming Mitsuhiro Yokoyama, Hideki Origasa, Masunori Matsuzaki, Yuji Matsuzawa and Yasushi Saito as inventors. A true and correct copy of the '537 patent is attached to this complaint as Exhibit C.

38. The '537 patent is assigned to Mochida Pharmaceutical Co., Ltd.

39. Amarin Pharma, Inc. holds an exclusive license to the '537 patent.

40. The '537 patent reflects and claims the analysis and outcome published in the Saito Article. *See, e.g.*, Ex. C at Example 1 (col. 13, ll. 1 to col. 15, ll. 61 (including the referenced tables and figures).

41. Claim 1 of the '537 patent recites as follows:

> 1. A method of reducing occurrence of a cardiovascular event in a hypercholesterolemia patient consisting of:
>
> identifying a patient having triglycerides (TG) of at least 150 mg/DL and HDL-C of less than 40 mg/dL in a blood sample taken from the patient as a risk factor of a cardiovascular event, wherein the patient has not previously had a cardiovascular event, and administering ethyl icosapentate in combination with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor,
>
> wherein said 3-hydroxyl-3-methylglutaryl coenzyme A reductase inhibitor is administered to the patient at least one of before, during and after administering the ethyl icosapentate; and
>
> wherein the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor is selected from the group consisting of pravastatin, lovastatin, simvastatin, fluvastatin, atorvastatin, pitavastatin, rosuvastatin, and salts thereof, and
>
> wherein daily dose of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor are 5 to 60 mg for pravastatin, 2.5 to 60 mg for simvastatin, 10 to 180 mg for fluvastatin sodium, 5 to 120 mg for atorvastatin calcium hydrate, 0.5 to 12 mg for pitavastatin calcium, 1.25 to 60 mg for rosuvastatin calcium, 5 to 160 mg for lovastatin, and 0.075 to 0.9 mg for cerivastatin sodium.

42. On February 4, 2014, the USPTO duly and legally issued the ’077, titled “Stable Pharmaceutical Composition and Methods of Using Same,” and naming Mehar Manku, Ian Osterloh, Pierre Wicker, Rene Braeckman, and Paresh Soni as inventors. A true and correct copy of the ’077 patent is attached to this complaint as Exhibit O.

43. The ’077 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

44. Amarin Pharma, Inc. holds an exclusive license to the ’077 patent.

45. Claims 1 and 8 of the ’077 patent recites as follows:

> 1. A method of reducing triglycerides in a subject with mixed dyslipidemia on statin therapy comprising, administering to the subject a pharmaceutical composition comprising about 2500 mg to 5000 mg per day of ethyl eicosapentaenoate and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters to effect a reduction in fasting triglyceride levels in the subject.
>
> 8. The method of claim 1 wherein the subject exhibits a reduction in hs-CRP compared to placebo control.

46. On February 25, 2020, the USPTO duly and legally issued the ’861 patent, titled “Methods of reducing the risk of a cardiovascular event in a subject at risk for cardiovascular

disease," and naming Paresh Soni as the inventor. A true and correct copy of the '861 patent is attached to this complaint as Exhibit P.

47. The '861 patent is assigned to Amarin Pharmaceuticals Ireland Limited.

48. Amarin Pharma, Inc. holds an exclusive license to the '861 patent.

49. Claims 1 and 2 of the '861 patent recite as follows:

> 1. A method of reducing risk of cardiovascular death in a subject with established cardiovascular disease, the method comprising administering to said subject about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death in the subject.
>
> 2. The method of claim 1, wherein the subject has a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL.

C. Amarin's VASCEPA® Receives FDA Approval for Reducing the Risk of Certain Cardiovascular Events in Patients with High Triglycerides and Low HDL-C Levels Concurrently on Statin Therapy

50. Amarin Pharmaceuticals Ireland Limited is the current holder of NDA No. 202057 for 1 g and 0.5 g icosapent ethyl capsules. Amarin Pharma, Inc. is Amarin Pharmaceuticals Ireland Limited's agent in the United States for purposes of communicating with the FDA regarding NDA No. 202057. Amarin Pharmaceuticals Ireland Limited and Amarin Pharma, Inc. market both strengths of the approved drug product under the tradename VASCEPA®.

51. A true, correct, and complete copy of the current FDA-approved Prescribing Information for VASCEPA®, covering both the 1 g and 0.5 g strengths, is attached as Exhibit D.

52. VASCEPA® is indicated as (1) an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia (the "Severe Hypertriglyceridemia Indication"), and (2) as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and

established cardiovascular disease or diabetes mellitus and 2 or more additional risk factors for cardiovascular disease (the "CV Indication"). Ex. D, § 1.

53. FDA first approved 1 g strength icosapent ethyl capsules, sold under the trade name VASCEPA®, pursuant to NDA No. 202057 on July 26, 2012.

54. A supplement to NDA No. 202057 for the 0.5 g strength of icosapent ethyl capsules was approved on February 16, 2017.

55. From July 26, 2012 through December 12, 2019, the sole indication for which VASCEPA® had received FDA approval was the Severe Hypertriglyceridemia Indication. FDA approval was based, in part, on the MARINE clinical trial and information from that trial is included on the VASCEPA® label. *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label).

56. From 2012 through December 12, 2019, the label for VASCEPA® contained the following limitation of use: "The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined" (the "CV Limitation of Use"). *See* Ex. E (VASCEPA® July 2012 label); Ex. F (VASCEPA® Feb. 2017 label). The CV Limitation of Use appeared in three places on the VASCEPA® label during that time period. *See* Ex. E at Highlights of Prescribing Information and Sections 1 and 14; Ex. F (same). The CV Limitation of Use as it appears in the VASCEPA® Label approved by FDA in February 2017 is reproduced below with annotations in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION

VASCEPA® (icosapent ethyl) Capsules, for oral use
Initial U.S. Approval: 2012

These highlights do not include all the information needed to us VASCEPA® safely and effectively. See full prescribing information fc VASCEPA.

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:
•The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

•The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined. (1)

Ex. F at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving VASCEPA and should continue this diet and exercise regimen with VASCEPA.

Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

Limitations of Use:

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 1.

VASCEPA 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with VASCEPA was not associated with elevations in LDL-C levels relative to placebo.

The effect of VASCEPA on the risk of pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Id. § 14.

57. The CV Limitation of use appearing on the VASCEPA® label from 2012 through December 12, 2019 was consistent with other products in the therapeutic category, such as LOVAZA®, a combination of ethyl esters of omega 3 fatty acids including EPA. To illustrate, the version of the LOVAZA® label approved by FDA on April 3, 2019 also contained the CV Limitation of Use, as shown below with an annotation in red:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOVAZA safely and effectively. See full prescribing information for LOVAZA.

LOVAZA (omega-3-acid ethyl esters capsules), for oral use
Initial U.S. Approval: 2004

----------INDICATIONS AND USAGE----------
LOVAZA is a combination of ethyl esters of omega 3 fatty acids, principally eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia (HTG). (1)

Limitations of Use:
- The effect of LOVAZA on the risk for pancreatitis has not been determined. (1)
- The effect of LOVAZA on cardiovascular mortality and morbidity has not been determined. (1)

Ex. S at Highlights of Prescribing Information.

58. On December 13, 2019, FDA approved VASCEPA® for the CV Indication, based on the results of the REDUCE-IT clinical trial. *See* Ex. G.

59. In conjunction with VASCEPA®'s approval for the CV Indication, the VASCEPA® label was modified to remove the CV Limitation of Use and add the CV Indication, among other changes. *Compare* Ex. D, *with* Exs. E and F.

60. To illustrate, the Highlights of Prescribing Information of the VASCEPA® label as approved by FDA in December 2019 lacks the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VASCEPA® safely and effectively. See full prescribing information for VASCEPA.

VASCEPA® (icosapent ethyl) capsules, for oral use
Initial U.S. Approval: 2012

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	12/2019
Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

----------INDICATIONS AND USAGE----------

VASCEPA is an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- as an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and
  - established cardiovascular disease or
  - diabetes mellitus and 2 or more additional risk factors for cardiovascular disease. (1)
- as an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

----------DOSAGE AND ADMINISTRATION----------

See Ex. D. This is in contrast with the 2019 LOVAZA® label which still contains the CV Limitation of Use. *See* Ex. S.

61. The current VASCEPA® label instructs, recommends, and encourages administering icosapent ethyl in combination with a statin to patients with baseline triglycerides ≥ 150 mg/dL to reduce the risk of a cardiovascular event in a daily dose of 4 grams per day. *See* Ex. D. Notably, FDA did not include an upper limit on the triglyceride range for the CV Indication.

62. FDA's December 13, 2019 approval of VASCEPA® for the CV Indication was hailed as "a major milestone in cardiovascular prevention." Ex. I. As the lead investigator for the REDUCE-IT study explained, "Nothing this significant has happened in the world of cardiovascular prevention since the introduction of statins nearly three decades ago. Many patients stand to benefit from this historic advance in care." *Id.*

63. On information and belief, following VASCEPA®'s approval for the CV Indication and the concurrent removal of the CV Limitation of Use from the VASCEPA® label, healthcare providers rapidly associated administration of icosapent ethyl together with a statin as a method for reducing risk of cardiovascular events in patients with baseline triglycerides ≥ 150 mg/dL.

64. On information and belief, Defendants learned that FDA approved VASCEPA® for the CV Indication on or around December 13, 2019 because, on information and belief, Defendants regularly monitor the approval status of brand-name drugs serving as the RLD for its generic drug candidates, and thus learned of VASCEPA® additional approval either from the FDA's press release announcing the same (Ex. J), Amarin's press release announcing the same (Ex. I), or in some other form.

D. Amarin Listed the Asserted Patents Patent in the FDA's Orange Book as Covering VASCEPA®

65. In conjunction with NDA No. 202057, Amarin submitted patent information relating to VASCEPA® to FDA for listing in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to the "Orange Book," which provides notice concerning patents covering FDA-approved drugs.

66. On January 9, 2020, Amarin timely submitted patent information regarding the '537 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

67. The ’537 patent was listed in the Orange Book on or about January 10, 2020 with patent use code U-2707, “Use of VASCEPA as an adjunct to statin therapy to reduce the occurrence of a cardiovascular event in an adult patient with hypercholesteremia.”

68. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’537 patent.

69. On January 6, 2020, Amarin timely submitted patent information regarding the ’077 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

70. The ’077 patent was listed in the Orange Book on or about January 6, 2020 with patent use code U-2693, “Use of VASCEPA to reduce triglycerides in a mixed dyslipidemia adult patient with elevated triglyceride (TG) levels (>= 150 mg/dL) and on statin therapy.”

71. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’077 patent.

72. On March 20, 2020, Amarin timely submitted patent information regarding the ’861 patent to FDA for listing in the Orange Book as covering methods of using VASCEPA® pursuant to 21 U.S.C. § 355(c)(2) and 21 C.F.R. § 314.53(d)(3).

73. The ’861 patent was listed in the Orange Book on or about March 20, 2020 with patent use code U-2756, “Use of VASCEPA as an adjunct to statin therapy to reduce the risk of cardiovascular death in an adult patient with established cardiovascular disease.”

74. Methods of using VASCEPA® (icosapent ethyl) capsules, 1 g and 0.5 g, for treating patients as provided in the VASCEPA® label are covered by at least one claim of the ’861 patent.

75. On information and belief, Defendants learned that Amarin listed the ’537, ’077, and ’861 patents in the Orange book as covering VASCEPA® at or around their time of listing in the

Orange Book because, on information and belief, Defendants regularly monitor the Orange Book for updated patent listings made for brand-name drugs serving as the RLD for their generic drug candidates.

ACTS GIVING RISE TO THIS ACTION FOR DEFENDANTS' INFRINGEMENT OF THE PATENT-IN-SUIT

76. The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the "Hatch-Waxman Act," amended the Federal Food, Drug, and Cosmetic Act ("FDCA") and governs approvals of generic drugs. Under Section 505(j) of the amended FDCA, codified at 21 U.S.C. § 355(j), companies wishing to bring a generic version of a branded prescription drug to market can submit an Abbreviated New Drug Application ("ANDA") to the FDA.

77. The ANDA process allows the generic drug company to avoid the expensive clinical trials required of an NDA holder to demonstrate a drug's safety and effectiveness by relying on the original NDA submission for that purpose. This process results in an enormous cost and time savings to the generic drug company. Reliance on the innovator company's data and the ability to "free ride" on the innovator company's development saves the generic drug company millions of dollars and years in development and clinical research costs.

78. The Hatch-Waxman Act also contains provisions meant to balance the competing interests of innovator and generic drug companies. When seeking ANDA approval, the generic applicant must consult the Orange Book and make certain certifications with respect to each patent listed for the branded drug. The generic applicant can certify that no patent information appears in the Orange Book ("Paragraph I certification"); that the listed patent has already expired ("Paragraph II certification"); that the applicant will not market the generic version before the date on which the patent will expire ("Paragraph III certification"); or that the patent is invalid or will

not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted ("Paragraph IV certification"). 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). When a Paragraph IV certification is made, the generic applicant must also provide notice of the certification to the innovator company, who can choose to enforce its patents in federal court.

79. When the listed patent is a method-of-use patent, like the Asserted Patents, the generic applicant can attempt to seek FDA approval to label its drug only for uses not covered by the patent, in which case a statement is submitted under 21 U.S.C. § 355(j)(2)(A)(viii), commonly known as a "Section viii statement" or "Section viii carve-out," in place of a patent certification. The generic applicant is not obligated to provide notice of a Section viii statement to the innovator company.

80. For an Orange Book-listed method-of-use patent that has not expired, whether to make a Paragraph III or Paragraph IV certification or a Section viii statement is a calculated business decision the generic applicant makes after evaluating the associated commercial risks.

81. It is the generic applicant's responsibility to ensure that the marketing and sale of its ANDA product (including the associated labeling, not limited to the Indications and Usage section) pursuant to a Section viii statement does not infringe the patents referenced in the Section viii statement. Indeed, FDA describes its role with respect to patents as "ministerial," has observed that it "lack[s] expertise in patent matters," and does not make patent infringement determinations when reviewing the labeling associated with a Section viii statement. 68 Fed. Reg. 36,683. Courts have found generic manufacturer's labels, approved subject to a Section viii statement, to nonetheless be evidence of patent infringement.

82. The Orange Book also contains therapeutic equivalence ratings for multisource prescription drug products. The agency developed these ratings in the 1970s in response to states

that requested guidance as they implemented laws to encourage generic substitution. FDA has explained that an AB rating reflects a decision that a generic drug is therapeutically equivalent to a branded drug when the generic drug is used as labeled, and it does not reflect a decision of therapeutic equivalence for off-label uses.

83. On information and belief, on or about September 21, 2016, Hikma (through its predecessor) submitted ANDA No. 209457 for generic copies of VASCEPA® (icosapent ethyl) 1 mg under section 505(j) of the FDCA.

84. On information and belief, Hikma Pharmaceuticals USA, Inc. is the current owner of ANDA No. 209457.

85. As an ANDA filer, Hikma was required to provide to FDA patent certifications or Section viii statements addressing each of the patents timely listed in the Orange Book for VASCEPA® before FDA finally approved ANDA No. 209457. 21 C.F.R. § 314.94(a)(12).

86. At the time the Asserted Patents were listed in the Orange Book, FDA had not yet finally approved ANDA No. 209457. Thus, before FDA's final approval of ANDA No. 209457 in May 2020, Hikma was required to provide to FDA either patent certifications or Section viii statements as to the Asserted Patents. 21 C.F.R. § 314.94(a)(12).

87. On information and belief, Hikma knew, at least because of the Asserted Patents' listing in the Orange Book as covering VASCEPA®, that use of icosapent ethyl just like VASCEPA® would constitute direct infringement of the Asserted Patents.

88. On information and belief, Hikma submitted to FDA Section viii statements with respect to the Asserted Patents after January 9, 2020 and before May 21, 2020.

89. On information and belief, on or about May 21, 2020, the FDA granted final approval for Hikma's ANDA No. 209457 with Section viii statements for the Asserted Patents, including labeling prepared by Hikma with full knowledge of the Asserted Patents.

90. On information and belief, a true and correct copy of Hikma's labeling that is provided with its icosapent ethyl capsules, and reflecting its Section viii statement strategy for the Asserted Patents, is attached hereto as Exhibit K ("Hikma's Label").

91. Like the current VASCEPA® label, Hikma's Label does not include the CV Limitation of Use. *Compare* Ex. D *with* Ex. K at Highlights of Prescribing Information and Sections 1 and 14. As shown below, the relevant sections of Hikma's Label lack the CV Limitation of Use:

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ICOSAPENT ETHYL CAPSULES safely and effectively. See full prescribing information for ICOSAPENT ETHYL CAPSULES.

ICOSAPENT ETHYL capsules, for oral use
Initial U.S. Approval: 2012

---------- **RECENT MAJOR CHANGES** ----------

Warnings and Precautions, Atrial Fibrillation/Flutter (5.1)	12/2019
Warnings and Precautions, Bleeding (5.3)	12/2019

---------- **INDICATIONS AND USAGE** ----------

Icosapent ethyl capsules are an ethyl ester of eicosapentaenoic acid (EPA) indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia. (1)

Limitations of Use:

- The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. (1)

---------- **DOSAGE AND ADMINISTRATION** ----------

Ex. K at Highlights of Prescribing Information.

1 INDICATIONS AND USAGE

Icosapent ethyl is indicated:

- as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Limitations of Use

The effect of icosapent ethyl on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Ex. K at § 1.

Icosapent ethyl 4 grams per day reduced median TG, VLDL-C, and Apo B levels from baseline relative to placebo. The reduction in TG observed with icosapent ethyl was not associated with elevations in LDL-C levels relative to placebo.

Ex. K at § 14.

92. On information and belief, from the time Hikma submitted ANDA No. 209457 to FDA in September 2016 and until Hikma submitted to FDA Section viii statements with respect to the Asserted Patents, the proposed label for Hikma's icosapent ethyl capsules prepared by Hikma contained the CV Limitation of Use. On information and belief, on or about the date on which it submitted to FDA Section viii statements with respect to the Asserted Patents, Hikma intentionally amended the proposed labeling for its icosapent ethyl capsules to remove the CV Limitation of Use. On information and belief, with knowledge of the Asserted Patents, Hikma removed the CV Limitation of Use from the Hikma Label so that healthcare providers and patients would believe that Hikma's generic icosapent ethyl capsules could be and should be used just like VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®. Hikma's removal of the CV Limitation of Use from the Hikma Label demonstrates Hikma's specific intent to induce infringement of the Asserted Patents.

93. On information and belief, Hikma has always intended for its icosapent ethyl capsules to be used in the place of VASCEPA® for all of VASCEPA®'s uses. On information and belief,

Hikma developed its product based on market assumptions that included the entirety of VASCEPA®'s sales, not just for sales resulting from treatment pursuant to the Severe Hypertriglyceridemia Indication.

94. On information and belief, Hikma was and is aware that over 75% of the sales of VASCEPA® since 2013 are for uses other than the Severe Hypertriglyceridemia Indication, including uses to reduce CV events. Ex. W (Nevada Case, D.I. 373) ¶ 115. At the trial concerning Hikma's infringement of the patents related to the Severe Hypertriglyceridemia Indication,[1] Hikma, through its counsel, repeatedly argued that the "vast majority" of prescriptions for VASCEPA® are for uses other than for the Severe Hypertriglyceridemia Indication. Ex. W (Nevada Case, D.I. 377) ¶ 440; Ex. AA (Nevada Case Trial Tr.) at 1252-1253 (Hoffman); *see also* Ex. Q (Nevada Case DDX 1-36); Ex. R (Nevada Case DDX 8.13). At trial in the Nevada Case, Hikma, through its counsel, acknowledged that there are "several reasons why a physician might prescribe Vascepa (or Defendants' ANDA Products) … other than to treat severe hypertriglyceridemia," including to reduce cardiovascular risk. Ex. W (Nevada Case, D.I. 377) ¶ 116.

95. On information and belief, Hikma is aware and intends that its generic product, which Hikma describes as AB rated to VASCEPA® for "hypertriglyceridemia," will be substituted for all VASCEPA® prescriptions, not just the prescriptions directed to the Severe Hypertriglyceridemia Indication. *See* Ex. T ("Hikma's Website").

96. Hikma Pharmaceuticals PLC issued a press release on March 31, 2020 referencing "Hikma's generic version of Amarin Corporation's Vascepa® (icosapent ethyl) 1 gm capsules."

[1] Amarin Pharma, Inc. et al. v. Hikma Pharmaceuticals USA, Inc. et al., Case No. 1:16-cv-02525-MMD-NJK (D. Nev.) [hereinafter the "Nevada Case"].

A true and correct copy of this press release, obtained from Hikma's website is attached hereto as Exhibit L ("Hikma's March 2020 Press Release").

97. In Hikma's March 2020 Press Release, Hikma stated that "Vascepa® is a prescription medicine that is indicated, *in part*, as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. According to IQVIA, US sales of Vascepa® were approximately $919 million in the 12 months ending February 2020." Ex. L (emphasis added).

98. The $919 million in Vascepa® sales referenced in Hikma's March 2020 Press Release includes sales for ***all uses*** of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of VASCEPA®'s sales).

99. Hikma's March 2020 Press Release does not state that Hikma's "generic version" of VASCEPA® should not be used for the CV Indication or that the effect of icosapent ethyl on cardiovascular mortality and morbidity had not been determined. *See* Ex. L.

100. Hikma's March 2020 Press Release communicates to and instructs healthcare providers and patients that Hikma's "generic version" of VASCEPA® ***should be used for all the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®, and thus promotes and encourages that use.

101. Hikma's March 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

102. On information and belief, in mid-October 2020, Hikma purported to remove the March 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the March 2020 Press Release encourages healthcare providers and patients to use Hikma's "generic version" of VASCEPA® for all the

same indications as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA® and as claimed in the Asserted Patents. However, Hikma's March 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2766/vascepa-press-release-positive-march-30-2020-720pmet-final.pdf.

103. Hikma Pharmaceuticals PLC issued a press release on September 3, 2020 referencing "Hikma's generic version of Vascepa® (icosapent ethyl) 1 gm [capsules]." A true and correct copy of this press release is attached hereto as Exhibit M ("Hikma's September 2020 Press Release").

104. In Hikma's September 2020 Press Release, Hikma stated that "Vascepa® is a prescription medicine that is indicated, *in part*, as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. According to IQVIA, US sales of Vascepa® were approximately $1.1 billion in the 12 months ending July 2020." Ex. M (emphasis added).

105. The $1.1 billion in Vascepa® sales referenced in Hikma's September 2020 Press Release includes sales for all uses of Vascepa®, including the CV Indication (which Hikma knew made up more than 75% of sales).

106. Hikma's September 2020 Press Release does not state that Hikma's "generic version" of VASCEPA® should not be used for the CV Indication or that the effect of icosapent ethyl on cardiovascular mortality and morbidity had not been determined. *See* Ex. M.

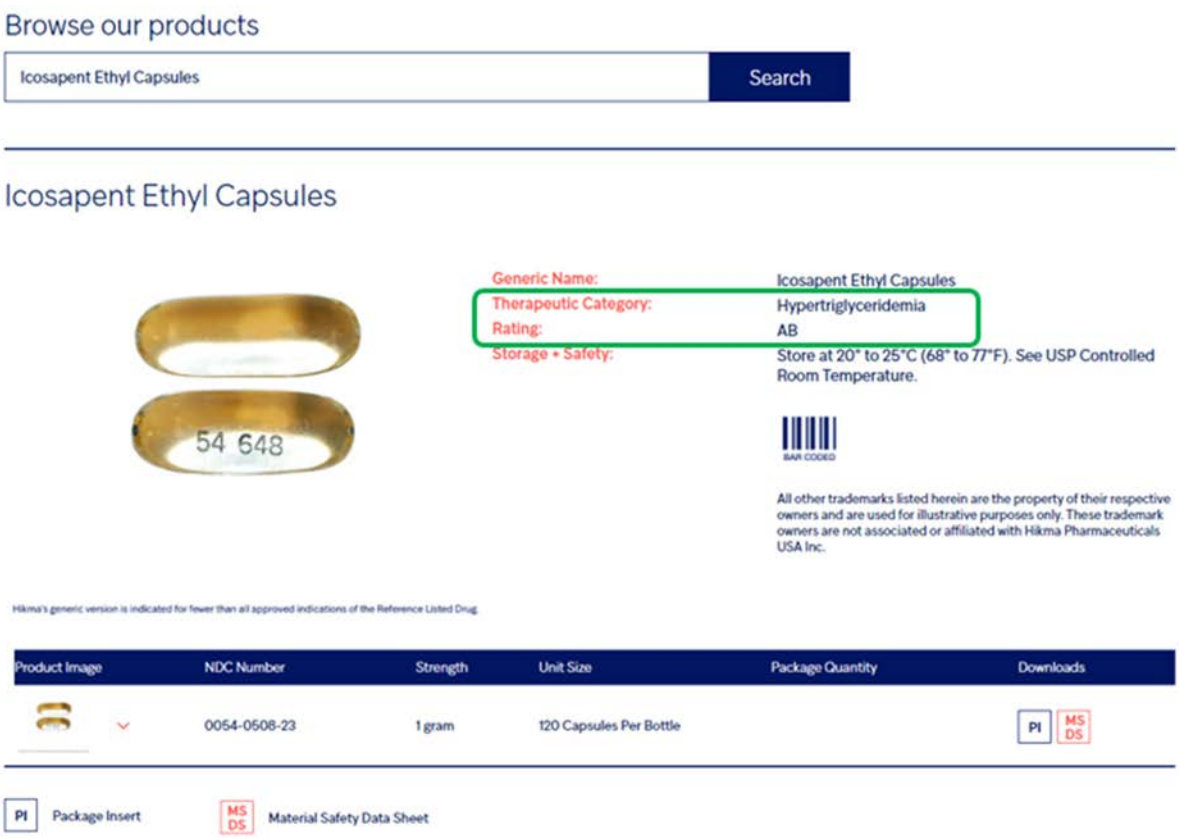
107. Hikma's September 2020 Press Release communicates to and instructs healthcare providers and patients that Hikma's "generic version" of VASCEPA® ***should be used for all the same indications*** as VASCEPA®, including to reduce the risk of CV events per the CV Indication

awarded to VASCEPA® and as claimed in the Asserted Patents, and thus promotes and encourages that use.

108. Hikma's September 2020 Press Release demonstrates Hikma's specific intent to encourage infringement of the Asserted Patents.

109. On information and belief, in mid-October 2020, Hikma purported to remove the September 2020 Press Release from the "Newsroom" page of its website. On information and belief, that action demonstrates Hikma's knowledge that the September 2020 Press Release encourages healthcare providers and patients to use Hikma's "generic version" of VASCEPA® for all the same indications as VASCEPA®, including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®. However, Hikma's September 2020 Press Release is still accessible as of November 30, 2020 on Hikma's website at the following URL: https://www.hikma.com/media/2836/vascepa-statement-september-2020-vfinal.pdf.

110. Further, Hikma has launched its generic version of VASCEPA® and promoted to the market, including on its website, that it is "AB" rated in the "Therapeutic Category: Hypertriglyceridemia." A copy of the product information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website is reproduced below with a green annotation.



See Ex. T.

111. Notably, the "Therapeutic Category" information for Hikma's Icosapent Ethyl Capsules communicated on Hikma's Website—"Hypertriglyceridemia"—does not match and is broader than the Indications and Usage sections of Hikma's Label, which includes only the Severe Hypertriglyceridemia Indication (i.e., triglycerides ≥ 500 mg/dL). Moreover, Hikma's Label does not include the CV Limitation of Use included on the original VASCEPA® label. *Compare* Ex. K, *with* Ex. E.

112. Hikma's March and September 2020 Press Releases, together with Hikma's Website that identifies and describes its generic version of VASCEPA® as "AB" rated in the therapeutic category "Hypertriglyceridemia," and the Hikma Label, instruct, promote, and encourage healthcare providers and patients to administer Hikma's generic icosapent ethyl capsules to

hypercholesterolemia patents with triglycerides of at least about 150 mg/dL and HDL-C of less than about 40 mg/dL and who are taking a statin, to reduce the risk of occurrence of a cardiovascular event, as covered by claims of the Asserted Patent.

113. As described above, the totality of Hikma's March 2020 Press Release and September 2020 Press Release, the Hikma Label, and the Hikma Website, instruct, promote, and encourage healthcare providers and patients to administer Hikma's icosapent ethyl capsules just like VASCEPA® including to reduce the risk of CV events per the CV Indication awarded to VASCEPA®.

114. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with, as determined by blood draw (*see, e.g.*, Ex. K, § 2 ("Assess lipid levels before initiating therapy.")), **(a)** a baseline total cholesterol level of ≥ 220 mg/dL, which a skilled artisan would recognize as signifying hypercholesterolemia (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "TG (mg/dL)" is 254)); **(b)** a baseline triglyceride level ≥ 150 mg/dL (*see, e.g.*, *id.* (for treatment group, "baseline" "TG (mg/dL)" is 680); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . .")); **(c)** a baseline HDL-C level less than 40 mg/dL (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27)); and who are **(d)** concomitantly receiving statin therapy, including for example 10-80 mg of atorvastatin (*see, e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"); *id.* § 12.3 ("Atorvastatin: In a drug-drug interaction study of 26 healthy adult subjects, icosapent ethyl 4 g/day at steady-state did not significantly change the steady-state AUC_{τ} or C_{max} of atorvastatin, 2-hydroxyatorvastatin, or 4-hydroxyatorvastatin when co-administered with atorvastatin 80 mg/day at steady state.")), and **(e)** have not had a previous

cardiovascular event (*see, e.g.*, *id.* at Patient Information leaflet ("Heart rhythm problems which can be serious and cause hospitalization have happened *in people who take icosapent ethyl, especially in people who have* heart (cardiovascular) disease or *diabetes with a risk factor for heart (cardiovascular) disease*, or who have had heart rhythm problems in the past.") (emphases added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information).")).

115. Like the VASCEPA® label, Hikma's Label encourages, promotes, and instructs treating patients who present with **(a)** established cardiovascular disease (*see, e.g.*, Ex. K at Patient Information leaflet ("Heart rhythm problems which can be serious and cause hospitalization have happened *in people who take icosapent ethyl, especially in people who have heart (cardiovascular) disease* or diabetes with a risk factor for heart (cardiovascular) disease, or who have had heart rhythm problems in the past.") (emphasis added); *id.* § 17 ("Advise the patient to read the FDA-approved patient labeling before starting icosapent ethyl (Patient Information)."), **(b)** a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL (*see, e.g.*, *id.* § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study . . . ."); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . .")), and **(c)** a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL (*see, e.g.*, *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)), **(d)** with about 4 g of icosapent ethyl (ethyl icosapentate) per day (*see id.* § 2.2)).

116. In addition, Hikma's 2020 Label states in its Patient Information leaflet: "Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet." *See* Ex. K. At trial, one of Hikma's physician experts pointed to this sentence during trial that "most

often we use this medication for reasons other than the MARINE data, and in the patient information section it specifically tells the patients that we would potentially do that." Ex. X (Nevada Case, Trial Tr.) at 617.

117. Thus, a healthcare provider with knowledge of the significance of FDA approving VASCEPA® for the CV Indication, and the consequential removal of the CV Limitation of Use from the VASCEPA® label in conjunction with that approval, the contents of Hikma's March and September 2020 Press Releases, Hikma's Website, and Hikma's Label, will inevitably practice at least the methods the '537 and '861 patents by administering icosapent ethyl to at least some patients with the characteristics required by those claims and at a dose of 4g per day, including for a period effective to reduce risk of cardiovascular death.

118. Like the VASCEPA® label, Hikma's Label encourages, promotes and instructs treating patients who present with **(a)** mixed dyslipidemia (*see, e.g.*, Ex. K, § 14.2 ("Patients whose baseline TG levels were between 500 and 2,000 mg/dL were enrolled in this study . . . ."); *id.* § 6.1 ("Hypertriglyceridemia Trials: In two randomized . . . trials in patients with triglyceride levels between 200 and 2000 mg/dL treated for 12 weeks [with icosapent ethyl]. . . ."); *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "LDL-C (mg/dL)" is 91)); *id.* § 14.2, tbl. 2 (for treatment group, "baseline" "HDL-C (mg/dL)" is 27), and **(b)** who are on statin therapy (*see, e.g.*, *id.* § 14.2 ("Twenty-five percent of patients were on concomitant statin therapy"), with **(c)** a pharmaceutical composition comprising about 4 g of icosapent ethyl (ethyl eicosapentaenoate) per day and not more than about 5%, by weight of all fatty acids, docosahexaenoic acid or its esters (*see, e.g.*, *id.* § 2.2; Nevada Case, D.I. 381 (Bench Order) at 8 ("The 'pharmaceutical composition' in Hikma's ANDA Product, if approved, will comprise 'at least about 96% by weight of all fatty acids present, ethyl eicosapentaenoate[,] and substantially no docosahexaenoic acid or its esters . . . ."), to **(d)**

effect a reduction in fasting triglyceride levels in the subject (*see, e.g.*, Ex. K at § 1 ("Icosapent ethyl is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.")); and **(e)** wherein the patients exhibit a reduction in hs-CRP compared to placebo control (*see, e.g.*, Ex. U (Ballantyne) at abstract, Fig. 3, 5.).

119. For all the reasons set forth above, Hikma knows of and specifically intends for healthcare providers to administer its icosapent ethyl capsules in the place of VASCEPA® and to practice the methods of the Asserted Patents by administering icosapent ethyl to at least some patients with the characteristics required by those claims in the dose and for the duration required by those claims, and for the purposes recited in those claims, and its labeling and marketing materials promote, encourage, and instruct healthcare providers to practice the methods of the Asserted Patents.

COUNT I

(Infringement of the '537 Patent Under 35 U.S.C. § 271(b))

120. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

121. On information and belief Defendants have been and are inducing others to infringe the '537 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patents with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin.

122. On information and belief, healthcare providers administering and/or patients using Defendants' generic version of Vascepa® capsules within the United States do so in combination with a statin to, among other reasons, reduce the occurrence of a cardiovascular event in the patient population recited in claim 1 of the '537 patent, and thus directly infringe at least one claim of the '537 patent.

123. On information and belief, Defendants possessed the specific intent to encourage direct infringement of the '537 patent. On information and belief, Defendants knew about the '537 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 121.

124. Alternatively, Defendants subjectively believed that there was a high probability that the use of icosapent ethyl capsules for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patents with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event, and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, was protected by a valid patent, and that the activities referenced in paragraph 121 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

125. On information and belief, Defendants knew that the administration or use of their generic version of VASCEPA® would be for reducing the occurrence of a cardiovascular event, including a fatal cardiovascular event, in hypercholesterolemia patents with triglycerides of at least 150 mg/dL, HDL-C of less than 40 mg/dL, who have not previously had a cardiovascular event

and are taking a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (i.e., a statin), including for example atorvastatin at a daily dose from 5 to 120 mg, by administering highly pure EPA in combination with the statin, and so would be an act of direct infringement of the '537 patent, and that the activities referenced in paragraph 121 would actively induce direct infringement of the '537 patent. On information and belief, despite such knowledge, Defendants have been and are actively inducing the infringement of the '537 patent by others.

126. On information and belief, Defendants will continue to induce infringement of the '537 patent unless and until enjoined by the Court.

127. As a result of Defendants' inducement of infringement of the '537 patent, Plaintiffs have suffered damages, including lost profits.

COUNT II

(Infringement of the '077 Patent Under 35 U.S.C. § 271(b))

128. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

129. On information and belief Defendants have been and are inducing others to infringe the '077 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce triglycerides in a subject with mixed dyslipidemia by administering about 4 g of ethyl eicosapentaenoate per day.

130. On information and belief, healthcare providers administering and/or patients using 4 g per day of Defendants' generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce fasting triglyceride and hs-CRP levels in patients with mixed dyslipidemia, and thus directly infringe at least claim 8 of the '077 patent.

131. On information and belief, Defendants possessed the specific intent to encourage direct infringement of the '077 patent. On information and belief, Defendants knew about the '077 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 129 (2 up from here).

132. Alternatively, Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of highly pure icosapent ethyl capsules for reducing fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia was protected by a valid patent, and that the activities referenced in paragraph 129 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

133. On information and belief, Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to reduce fasting triglyceride and hs-CRP levels in subjects with mixed dyslipidemia, and so would be an act of direct infringement of the '077 patent, and that the activities referenced in paragraph 129 would actively induce direct infringement of the '077 patent. On information and belief, despite such knowledge, Defendants have been and are actively inducing the infringement of the '077 patent by others.

134. On information and belief, Defendants will continue to induce infringement of the '077 patent unless and until enjoined by the Court.

135. As a result of Defendants' inducement of infringement of the '077 patent, Plaintiffs have suffered damages, including lost profits.

COUNT III

(Infringement of the '861 Patent Under 35 U.S.C. § 271(b))

136. Plaintiffs incorporate each of the preceding paragraphs as if fully set forth herein.

137. On information and belief Defendants have been and are inducing others to infringe the '861 patent in this District and elsewhere in the United States by making, offering to sell, selling, importing, and otherwise promoting and distributing highly pure icosapent ethyl capsules to reduce the risk of a cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, by administering about 4 g of ethyl icosapentate per day for a period effective to reduce risk of cardiovascular death.

138. On information and belief, healthcare providers administering and/or patients using 4 g per day of Defendants' generic version of Vascepa® capsules within the United States do so, among other reasons, to reduce the risk of cardiovascular death in patients with established cardiovascular disease, including the patient population recited in claims 1 and 2, and thus directly infringe at least claim 1 and 2 of the '861 patent.

139. On information and belief, Defendants possessed the specific intent to encourage direct infringement of the '861 patent. On information and belief, Defendants knew about the '861 patent at least as of when it was listed in the Orange Book and before performing the activities referenced in paragraph 137.

140. Alternatively, Defendants subjectively believed that there was a high probability that the administration and use of 4 g per day of icosapent ethyl capsules for reducing risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, was protected by a valid patent, and that the activities referenced in

paragraph 137 would actively induce infringement of the patent, but took deliberate steps to avoid confirming those facts, and therefore willfully blinded themselves to the infringing nature of their sales of a generic version of VASCEPA®.

141. On information and belief, Defendants knew that the administration or use of their generic version of VASCEPA® would be for daily administration of a 4 g/day dose to reduce risk of cardiovascular death in a subject with established cardiovascular disease, including subjects with a fasting baseline triglyceride level of about 135 mg/dL to about 500 mg/dL and a fasting baseline LDL-C level of about 40 mg/dL to about 100 mg/dL, for a period effective to reduce risk of cardiovascular death, and so would be an act of direct infringement of the '861 patent, and that the activities referenced in paragraph 137 would actively induce direct infringement of the '861 patent. On information and belief, despite such knowledge, Defendants have been and are actively inducing the infringement of the '861 patent by others.

142. On information and belief, Defendants will continue to induce infringement of the '861 patent unless and until enjoined by the Court.

143. As a result of Defendants' inducement of infringement of the '861 patent, Plaintiffs have suffered damages, including lost profits.

JURY TRIAL DEMAND

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs hereby demand a trial by jury of all issues so triable.

PRAYER FOR RELIEF

Plaintiffs respectfully pray for the following relief:

a) Enter judgment that Defendants have induced the infringement of the ’537, ’077, and ’861 patents by making, selling, offering to sell and importing generic icosapent ethyl capsules in or into the United States;

b) Issue an injunction under 35 U.S.C. § 283 permanently enjoining Defendants, their officers, agents, servants, employees, licensees, representatives, and attorneys, and all other persons acting or attempting to act in active concert or participation with them or acting on their behalf, from, directly or indirectly, making, selling, offering to sell, and importing into the United States any drug product for a use that is covered by the ’537, ’077, and ’861 patents;

c) Award Plaintiffs damages in an amount sufficient to compensate them for Defendants’ infringement of the ’537, ’077, and ’861 patents, together with prejudgment and post-judgment interests and costs under 35 U.S.C. § 284;

d) Declare this to be exceptional case under 35 U.S.C. § 285 and award Plaintiffs their reasonable attorneys’ fees, expenses, and costs incurred in this action;

e) Perform an accounting of Defendants’ infringing activities through trial and judgment; and

f) Award Plaintiffs such other and further relief as this Court deems just and proper.

Dated: November 30, 2020

FISH & RICHARDSON P.C.

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